IN THE CLAIMS:

See Listing of Claims attached hereto which will replace all prior versions of claims in the application.

Currently amended: Claims 44, 45, 47-49, 51-53, 55, 57, 60, 66 and 67.

Canceled: Claims 1-43, 46, 50, 61.

Previously presented: Claims 54, 56, 62-65.

REMARKS

The Applicants acknowledge the Office Action of December 6, 2005, with appreciation. To begin, the Office acknowledges the Applicant's election of Restriction Group I, with traverse, with the Response and Election of September 2, 2005. The Office has made the restriction final. The Office indicates that Claims 44-86 are pending, of those, Claims 58-59 and 67-86 are withdrawn from consideration as being drawn to non-elected inventions. Claims 44-57 and 60-66 are currently under consideration.

The Office raises an objection to Claim 66 for reciting language which refers to non-elected inventions. With the instant Response and Amendment, Claim 66 is amended to remove the language drawn to a transformed host cell. The Applicants submit that the amendment removes the Office basis for the objection. Reconsideration and withdrawal of the objection is respectfully requested.

Claims 44, 46-50 and 60-66 are rejected for failing to comply with the written description requirement under 35 U.S.C. § 112, first paragraph. The claims are drawn to a method of generating or increasing a cytotoxic T cell response against an infectious agent or a tumor cell by administering an enterobacterium OmpA, or a

fragment thereof. The Office concludes that claims drawn to "a fragment thereof" of an OmpA protein encompass a genus of variant species for which the claimed immunogenic activities have not been demonstrated in a representative number of species.

With the Response and Amendment, the claims are amended to remove the language drawn to "fragments thereof" and generic Claim 44 is further amended to define the enterobacterium OmpA protein as comprising the sequence set forth in SEQ ID NO:2. Specificational support for the amendment may be found at page 6, lines 17-21. Claim 50 is presently canceled as being redundant on the generic claim. The Applicants submit that an enterobacterium OmpA protein, comprising the sequence set forth in SEQ ID NO:2, is described with particularity, and therefore, provides the requested definition. Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 44, 46-50 and 60-66 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. There are several aspects to the rejection. It is the position of the Office that the Applicants have failed to demonstrate that the OmpA protein, or a fragment thereof, is capable of generating or increasing the claimed immune response to any infectious agent or tumor cell.

With the instant Response, the Applicants amend the generic scope of the claims to methods for generating or increasing a cytotoxic T cell response against a tumor cell. Consequently, the claim language drawn to increasing a cytotoxic T cell response to infectious agents has been removed from Claims 44, 45 and 51; Claims 46 and 61 are presently canceled. The Applicants further amend Claim 44 to include language to indicate that the pharmaceutical composition comprises an OmpA protein, having the sequence set forth in SEQ ID NO:2, in combination with a tumor antigen. Support for the amendment may be found in the instant Specification at page 4, line 35, and continuing to page 5.

The Applicants submit that the instant Specification provides an enabling disclosure for methods of generating or increasing a cytotoxic T cell response against a tumor

cell. The Applicants disclose methods of administration of an OmpA protein in combination with a tumor antigen and disclose methods for analysis of the claimed response. In Examples 4 and 6, the Applicants demonstrate that a tumor-specific CTL response is generated by the administration of an OmpA protein in combination with a tumor antigen. Furthermore, an associative antitumor effect is exhibited with the increased cytotoxic T cell response as demonstrated in Example 5. Therefore, the Applicants submit that the Specification provides enablement for methods of generating or increasing a cytotoxic T cell response against a tumor cell.

With regard to the rejection of Claims 60-64, the Office indicates that methods utilizing peptides comprising SEQ ID NO:4 and recombinant p40 (OmpA) to reduce the viability of tumor cell based xenographs in immunodeficient mice are enabled; however, the Office concludes that the Specification and examples do not provide enablement for the full scope of the invention, namely, the treatment or prevention of cancer in an immunocompetent animal.

The Applicants rebut the Office rejection for lack of enablement for claims to the treatment or prevention of cancer in an immunocompetent animal, including a human, according to the following arguments and supporting evidence. With regard to the Office basis for the rejection relying on the immunocompetence of the animal, the Applicants clarify that the animals of the instant *in vivo* model of tumorigenesis are immunocompetent. Therefore, enablement for the treatment or prevention of cancer in an animal, including an immunocompetent animal, may be found in Example 5. The Applicants submit that, based on the Specificational disclosure, those skilled in the art are apprised of methods of administration and dosage to elicit the claimed response, which methods may be extrapolated to any subject animal, including a human, and would require only routine experimentation.

With regard to enablement for Claims 60-64, drawn to methods for the treatment or prevention of cancer in an animal, including a human, the Applicants rely on the skill of those in the art of tumor immunotherapy, including those who conduct human clinical trials to evaluate immunotherapeutic technologies for the treatment or prevention of cancer. The Applicants discuss, at page 2 of the instant Specification,

the understanding of those skilled in the art with respect to the therapeutic potential of cytotoxic T lymphocytes (CTLs) in antitumor responses and discuss various vaccination strategies which are understood by those skilled in the art to induce an effective CTL response against a tumor cell. Moreover, it is well settled that the USPTO is not the FDA and may not require clinical testing to substantiate that which is known in the art.

The Applicants provide herewith a reference to Thurner, et al. (J. Exp. Med. 1999, 190:1669-1678) as an example of the understanding of those skilled in the art at the time of the invention with regard to tumor immunotherapy for the treatment or prevention of cancer in human patients. Thurner, et al. disclose that it has been established that CTLs can recognize tumor antigens and kill tumors (page 1669, first paragraph). Thurner, et al. discuss the functional significance of tumor-specific CTL responses in cancer immunotherapy and demonstrate favorable antitumor clinical responses through expansion of tumor-specific T cells in humans. Thurner, et al. demonstrate tumor regressions and attribute the tumor regression to the induction of tumor-specific CTLs (page 1676, right column, first paragraph). Therefore, Thurner, et al. establish the understanding of those skilled in the art with regard to the correlation between tumor regression and T cell responses, which responses are demonstrated in humans. Moreover, the Applicant's demonstration of an increased CTL response and associative antitumor efficacy is consistent with such correlation as to establish predictability in the art. Accordingly, those skilled in the art would readily accept that the instant *in vivo* models correlate with established methodology for treating or preventing human tumors through immunotherapy techniques which endeavor to increase cytotoxic T cell responses and promote tumor regression. Consequently, the Applicants submit that the instant Specification provides one skilled in the art with an enabling disclosure for the treatment or prevention of cancers in animals, including humans. Reconsideration and withdrawal of the rejection is respectfully requested.

Moving on, the Office rejects the claims as being anticipated under 35 U.S.C. § 102 over prior art which are alleged to disclose compositions comprising an

enterobacterium OmpA protein for inducing an immune response. With the instant Response, the Applicants amend the generic scope of the claims to a method for generating or increasing a cytotoxic T cell response to a tumor cell by administration of an OmpA protein in combination with a tumor antigen. The Applicants submit that the instant amendment removes the Office bases for rejection of the claims under 35 U.S.C. § 102. The Applicants discuss the individual rejections as follows.

The Office rejects Claims 44-46 and 48-52 under 35 U.S.C. § 102(b) over Rauly, et al., (Research in Immunology, 1998, Vol 149(1), page 99). The Office finds that Rauly, et al. teach compositions comprising an OmpA protein and a B-cell epitope, derived from Respiratory Syncytial Virus, which is administered to induce a CTL response against an infectious agent, and consequently, anticipates the instant claims.

The claims, as presently amended, are drawn to administration of an OmpA protein in combination with a tumor antigen to generate a CTL response against a tumor cell. The instant invention is distinguished on the basis that Rauly, et al. does not disclose tumor antigens, and is silent as to methods for generating or increasing a cytotoxic T cell response against a tumor cell. Consequently, the cited prior art does not teach or suggest all the claim limitations, and therefore, does not support a rejection for anticipation. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) is respectfully requested.

The Office rejects Claims 44-55, 57, 60-61 and 65 under 35 U.S.C. § 102(e) as being anticipated by Binz, et al., (U.S. Patent No. 6,197,929). The Office finds that Binz, et al. disclose an OmpA protein as a carrier protein to elicit a cytotoxic T cell response against a co-administered antigen, which antigen may originate from viruses.

With the instant amendment, claims are drawn to a method for generating or increasing a cytotoxic T cell response against a tumor cell by administering an OmpA protein in combination with a tumor antigen. The Applicants rebut the instant rejection for anticipation as per the previous discussion, inasmuch as Binz, et al.

does not disclose tumor antigens, nor methods of generating or increasing a cytotoxic T cell response against a tumor cell. The Applicants submit that the instant amendment removes the Office basis for the rejection over the Binz, et al. disclosure. Reconsideration and withdrawal of the rejection is respectfully solicited.

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Accordingly, entry of the present amendment into the record of this application, reconsideration of all grounds of objection and rejection, withdrawal thereof, and passage of this application to issue are all hereby respectfully solicited.

Respectfully submitted,

THE FIRM OF HUESCHEN AND SAGE

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Enclosure: Listing of Claims; Extension of Time Fee, one (1) month, check in the amount of $120.00; Form PTO-1449, listing one (1) reference and copy thereof and Postal Card Receipt.

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THE COMMISSIONER IS HEREBY AUTHORIZED TO CHARGE ANY FURTHER OR ADDITIONAL FEES WHICH MAY BE REQUIRED (DUE TO OMISSION, DEFICIENCY, OR OTHERWISE), OR TO CREDIT ANY OVERPAYMENT, TO DEPOSIT ACCOUNT NO. 08,3220.